

Exposure Estimates to Disinfection By-products of Chlorinated Drinking Water

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Exposure to disinfection by-products (DBPs) of drinking water is multiroute and occurs in households serviced by municipal water treatment facilities that disinfect the water as a necessary step to halt the spread of waterborne infectious diseases. Biomarkers of the two most abundant groups of DBPs of chlorination, exhaled breath levels of trihalomethanes (THMs) and urinary levels of two haloacetic acids, were compared to exposure estimates calculated from in-home tap water concentrations and responses to a questionnaire related to water usage. Background THM breath concentrations were uniformly low. Strong relationships were identified between the THM breath concentrations collected after a shower and both the THM water concentration and the THM exposure from a shower, after adjusting for the postshower delay time in collecting the breath sample. Urinary haloacetic acid excretion rates were not correlated to water concentrations. Urinary trichloroacetic acid excretion rates were correlated with ingestion exposure, and that correlation was stronger in a subset of individuals who consumed beverages primarily within their home where the concentration measurements were made. No correlation was observed between an average 48-hr exposure estimate and the urinary dichloroacetic acid excretion rate, presumably because of its short biological half-life. Valid biomarkers were identified for DBP exposures, but the time between the exposure and sample collection should be considered to account for different metabolic rates among the DBPs. Further, using water concentration as an exposure estimate can introduce misclassification of exposure for DBPs whose primary route is ingestion due to the great variability in the amount of water ingested across a population. **Key words:** biomarkers, chlorinated drinking water, exhaled breath, exposure, haloacetic acids, ingestion, shower, trihalomethane. *Environ Health Perspect* 107:103–110 (1999). [Online 11 January 1999] <http://ehpnet1.niehs.nih.gov/docs/1999/107p103-110weisell/abstract.html>

Exposures to compounds in residential drinking water occur through multiple routes and vary across the population because of differences in the amount and ways people use water. Common uses of water and their corresponding exposures include consumption of water directly and in prepared beverages or food (ingestion exposure); washing, bathing, showering, and swimming (dermal and inhalation exposure); in dishwashers, washing machines, and humidifiers (inhalation exposures). Municipal water in the United States is disinfected, with chlorine being the most common disinfectant agent. Disinfection of water, in addition to having the benefit of destroying microbes that can transmit diseases, has the drawback of producing a series of compounds known as disinfection by-products (DBPs) (1). Chlorination produces many compounds containing chlorine and/or bromine, some of which have been shown to be carcinogenic, mutagenic, and/or teratogenic in animal studies (2–6). The two most abundant classes of DBPs that result from chlorination of drinking water are trihalomethanes (THMs) and haloacetic acids (HAAs) (7). The THMs [chloroform (CHCl₃), bromodichloromethane (BDCM), chlorodibromomethane (CDBM), and bromoform (CHBr₃)] are volatile compounds. The

sum of their concentrations sometimes exceeds the national standard of 100 µg/l in drinking water samples. The HAAs (mono-, di-, and trichloroacetic acids, mono- and dibromoacetic acids, and mixed chloro- and bromoacetic acids) are nonvolatile compounds that also have exceeded 100 µg/l in some samples of drinking water. Dichloroacetic acid (DCAA) and trichloroacetic acid (TCAA) are the two most abundant HAAs in most water supplies (7).

To limit exposure to these compounds, the EPA (8) has regulated the total trihalomethane (TTHM) concentration. The current standard for TTHMs is 100 µg/l in the average of samples collected within the drinking water systems during four consecutive quarters. A proposal to lower that standard is under review with an initial Stage 1 proposal target value of 80 µg/l. In addition, a drinking water standard of 60 µg/l is being proposed for the sum of the five most prevalent HAAs (mono-, di-, and trichloroacetic acids and mono- and dibromoacetic acids) in the average of four consecutive samples. Future decreases, during Stage 2 regulation, of the TTHMs and HAAs to 40 µg/l and 30 µg/l, respectively, are being proposed.

To evaluate whether the adverse effects of exposure to chlorinated DBPs observed in animals also occur in humans at drinking water levels, epidemiological studies have been conducted. Some studies have found a number of health effects in people associated with exposure to chlorinated drinking water, including bladder cancer, renal cancer, and reproductive and developmental effects (9–13). However, other epidemiological studies have failed to find an association with these health end points and exposure to chlorinated water (10,14). The exposure estimates used in some of the aforementioned studies have taken the simplistic approach of assigning exposure based on whether the area in which an individual lived received chlorinated water or not. Other studies have followed a somewhat more elaborate approach of assigning exposure estimates based on the amount of chlorine used by the treatment plant or the concentration of TTHMs measured at different treatment plants in the study area during specified time periods. Misclassifications of exposures exist in these studies, reducing precision and reliability of the findings. More recently questionnaire data have been used to determine water use patterns and combined with historic water concentrations to estimate exposures to DBPs (15–19).

TTHM concentration measured once a quarter or the amount of chlorine added to the water at the treatment plant is an inaccurate assessment of exposure because the DBP concentrations in the water delivered to a home change spatially and temporally in a nonuniform fashion in the distribution system (20,21). The concentrations of individual DBPs produced during chlorination, while related to the amount of chlorine added and the amount of organic matter in the source water, can vary greatly depending upon the particular conditions at the treatment plant (22,23). For brominated compounds, the amount of bromide in the

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source water is an important factor in their production relative to chlorinated species. Further, it is unknown which DBPs, if any, are responsible for adverse health effects. The concentration of individual DBPs can vary relative to each other. Thus, the TTHM concentration or amount of chlorine added may not be correlated with the concentration of the biologically active DBPs.

Water use varies across individuals, and exposure to DBPs is multiroute, with the significance of each route dependent on the physicochemical property of each DBP and the activity patterns of the individual (24). Ignoring the manner in which water is used greatly increases the uncertainty in the exposure estimate. Variations exist in the amount of water consumed, the source of water consumed (tap, filtered, or bottled water may be drunk or used in preparing beverages and food), and the frequency and duration of bathing and showering. All these activities contribute to exposure. Thus, individuals living in residences with nearly identical DBP water concentrations can have vastly different exposures. Reif et al. (25) have suggested that an improved exposure assessment can be obtained from using tap water samples collected from subjects' homes and interviewing subjects to collect relevant data concerning patterns of water use and routes of exposure, including use of water filter systems, frequency and duration of bathing and showering, and water consumption rate.

The current study evaluated how well drinking water concentrations measured within homes correlated with biomarker concentrations and whether an improvement in the association is achieved using exposure estimates based on the water concentrations combined with questionnaire data about activities surrounding water uses. Two sets of biomarkers were examined. The first was exhaled breath measurement of the THMs at the time of the visit and after the subject showered the morning or evening prior to a visit. The second was urinary DCAA and TCAA excretion rates and creatinine-normalized concentrations. Prior studies, such as the Total Exposure Assessment Methodology (TEAM) study demonstrated that exhaled breath concentrations of chloroform and dichlorobromomethane, the two most abundant THMs, were correlated with drinking water concentrations of THMs in the home (26). Exhaled breath concentrations have been shown to be elevated following showering but not following ingestion because of variations in the degree of metabolism following different exposure routes (27). No previous study has examined the relationship between HAA exposures from drinking water and

their excretion rates, although a correlation between urinary TCAA and water concentrations of trichloroethene and tetrachloroethene, which are metabolized to TCAA, have been documented, and the authors indicated that a confounder to their results could be the presence of HAAs in the water resulting from chlorination (28,29).

Methods

Study design. We recruited 49 female subjects who had previously participated in a case-control study on neural tube birth defects and had a variety of potential exposures to chlorination DBPs, based on previously measured total THM concentrations in the tap water of each household (30). The subjects included individuals throughout the state of New Jersey, thus, they had received water from different water sources. The selection of subjects provided a wide range of HAA and THM exposures within the home rather than a distribution of exposures that might exist in either a single water distribution system or within the general population. Before a home visit, a new Tedlar (DuPont, Wilmington, DE) bag and urine sample collection vessel were sent to each subject with instructions on how to collect a postshower breath sample the evening or the morning before the visit and a first morning urine sample. Each subject was telephoned the day before the home visit as a reminder to collect the breath and urine samples. The subject recorded the collection time of the postshower breath sample, the shower duration, the shower water temperature (hot, warm, or cold), the time of urine collection, and the time of the previous urination. During the home visit, the Tedlar bag and urine samples were retrieved; a background breath sample, a time of visit urine sample, an air sample, and a cold tap water sample were collected; and a 48-hr recall questionnaire was administered. The data collection was conducted between 7 February 1995 and 6 February 1996 in New Jersey.

Postshower exhaled breath samples. Postshower whole-breath samples were collected by having the subject blow into a Tedlar air sampling bag at the completion of a shower. To quantify the breath levels, 1–2 liters of the breath were transferred onto a Carboxen 569 (Supelco, Inc., Bellefonte, PA) adsorbent trap using a personal sampling pump at a flow rate of 1 l/min as soon as the bag was returned to the laboratory. Storage tests demonstrated that the THMs were stable in the sampling bag for up to 48 hr. The breath samples were analyzed by thermal desorption coupled to gas chromatography/mass spectrometry (GC/MS) (31).

Background breath samples. To determine the background breath levels, alveolar breath samples were collected at the time of the visit using a portable system that composites exhaled breath over several minutes (31,32). Carboxen 569 was used as the adsorbent, and the sample was collected for 2 min at a flow rate of 1.5 l/min. The samples were analyzed for THMs by thermal desorption coupled to GC/MS.

Urine samples. Entire urine voids were collected in 500-ml polycarbonate or linear high-density polyethylene containers and stored in a refrigerator (4°C) until extraction, within 48 hr of collection. TCAA concentrations were constant, but DCAA concentrations decreased by 16% in 48 hr based on a single laboratory test. No correction for losses during storage was applied to the data. The volume of each urine sample was measured in the laboratory. The DCAA and TCAA concentrations were determined on 5-ml urine samples by extraction with ethyl ether and derivatization with 10% sulfuric acid in methanol, followed by GC/electron capture detector (ECD) (33). To correct for variations in the volume of urine excreted, creatinine was also analyzed in the urine using a calorimetric method based on its reaction with sodium picrate and absorption at 530 nm (34,35).

The entire first morning urine void was collected from each individual. The total amount (nanograms) of TCAA and DCAA excreted in a urine void was calculated by multiplying their concentrations in the urine by the volume of the urine void. The excretion rate was then calculated by dividing the total amount of TCAA or DCAA in the urine void by the time interval between the first morning urine void and the previous urination.

Water samples. Duplicate water samples were collected into clean 40-ml glass vials without any headspace from the cold water kitchen faucet, after allowing the water to run for approximately 1 min. The vials were immediately sealed with Teflon-faced (DuPont) septa screw top closures. The water samples were stored in a cooler with blue ice packs immediately after collection. In homes where a water filter system was installed on the kitchen faucet, water samples were taken from the bathroom if a filter system was not installed there. Chlorine residual was not quenched, but rather the samples were extracted within 24 hr, a time period during which controlled studies showed that no changes in the DBP concentrations occurred in water stored at 4°C.

THMs were analyzed on 5 or 10 ml of water by purge and trap using 0.6 g of Carboxen 569 in the adsorbent trap and

helium flowing at 40 ml/min for 20 min as the purge gas (36). The adsorbent trap was analyzed by thermal desorption coupled to GC/MS. Aliquots of the water (5 ml) were analyzed for DCAA and TCAA using liquid-liquid extraction into methyl *tert*-butyl ether followed by derivatization by 10% sulfuric acid in methanol. The extract was analyzed by GC/ECD (33).

Air samples. A 15-min indoor air sample was collected onto an adsorbent trap containing 0.6 g Carboxen 569 attached to a portable constant flow pump set at a flow rate of 1.0 l/min. No breakthrough of any of the THMs was found for these conditions. The air sample was analyzed for the four THMs using thermal desorption coupled to GC/MS.

Questionnaire. Each subject answered a 48-hr recall questionnaire during the home visit. Questions related to water use included whether a water filter system was used in the home; types and amounts of liquids consumed during the previous 48 hr; water use for cooking; frequency and duration of showers or baths; and frequency and duration of swimming or staying in a pool area. Questions related to the subjects' activities included amount of time the subject worked outside the home and activities that might contribute to the body burden of biomarkers measured, such as visits to locations that use chlorinated solvents that are metabolized to DCAA or TCAA.

Specific information was gathered about the types (tap water, bottled water, hot tea, soup, fruit drinks from frozen concentrate or powder, iced tea, iced coffee) and amounts (small, medium, large servings and consumption frequency) of liquids. The liquids were classified as either hot or cold liquids. Hot liquids included hot coffee, hot tea, and soup prepared with tap water. Cold liquids included tap water, fruit juices or drinks from frozen concentrate, fruit drinks from powder, iced tea, and iced coffee. Iced tea and iced coffee can be prepared using either hot water or cold water, and in both cases, ice is added, which can be considered a cold water contribution. Only five subjects consumed either iced tea or iced coffee, thus any error introduced by the above assumption is expected to be small.

To assess the thermal stability of DCAA and TCAA in hot beverages, we assumed that water is usually boiled for 5 min when preparing hot drinks such as coffee, tea, or soup. To simulate this procedure, 500 ml of water was boiled in a 1-liter Erlenmeyer flask on a hot plate for 5 min. The concentrations of DCAA and TCAA in the water were determined before and after the 5-min boiling, and the final

volume of water was also measured. This procedure was repeated four times, and average correction factors were calculated to estimate DCAA and TCAA ingestion exposures for hot liquids.

Quality control and quality assurance of the samples. The state of each instrument used was checked daily before use. The response of the instrument was verified to be within preestablished criteria. The calibration curves were prepared using external standards and checked daily using a solution containing a known quantity of the target compounds. The acceptance criteria for calculated concentrations of the known solution were $\pm 20\%$. When the criteria were not met, a new calibration of the instrument was prepared for each chemical. We maintained quality control charts of the instruments' responses. Blank adsorbent traps were transported and analyzed along with the sample traps on all field collection days. Duplicate samples were collected and analyzed from 10% of the homes. Calibration of sampling pumps was done before and after each use. Water and urine samples were extracted within 24 and 48 hr, respectively, with cold transport and storage. An internal standard, 2-bromopropionic acid, was used to check the efficiency of HAA extraction from water and urine samples.

Statistical analyses. Statistical differences between the low and high exposure groups were tested using the nonparametric Mann-Whitney test since the data were not normally distributed. Correlation analyses and linear regression analyses were conducted to examine the association between the biomarker levels (breath and urine concentrations) and both the water concentration and calculated exposure. For the above statistical procedures, $p \leq 0.05$ was set as the criterion for the significance of a test.

Results and Discussion

Water concentration. The water concentrations measured for the THMs and for TCAA and DCAA indicated that households with a range of concentrations were obtained (Table 1). The concentrations of

monochloroacetic acid, mixed chlorobromoacetic acids, and bromoacetic acids were uniformly low in almost all of the samples and so were not included in the exposure analysis. The water concentration distribution was bimodal, with approximately equal numbers of homes having TTHM and HAA water concentration above and below 10 $\mu\text{g/l}$. This distribution was the result of the selection criteria for choosing an equal number of homes at the extremes of the TTHM concentrations measured previously. The distribution of water concentrations, while not being representative of homes in New Jersey, provided a realistic range of environmental concentrations to determine whether a DBP exposure/biomarker relationship exists and whether water concentration approximates exposure.

THMs exposures and biomarkers. The majority of the background exhaled breath concentrations for each of the four THMs were below the study's detection limit of 1 $\mu\text{g/m}^3$. These breath concentrations are lower than previously reported in New Jersey during the TEAM study, which had a median value of 3.5 $\mu\text{g/m}^3$ obtained from 49 samples collected from nine subjects (37). One possible explanation for the difference between the two studies is the higher water concentrations of THMs measured during the TEAM study, which reported a median chloroform value of 128 $\mu\text{g/l}$ and a range of 11–225 $\mu\text{g/l}$, while in the current study, only 4 of the 49 values exceeded 120 $\mu\text{g/l}$. This decrease in TTHM water concentration reflects the New Jersey water purveyors' efforts to comply with the current standard and their general efforts to reduce the contaminant levels in the water that they provide to the public. In the present study, only nine exhaled breath samples were above the detection limit for chloroform. Fewer breath samples had detectable levels of the other THMs (four for BDCM, one for CDBM, and one for CHBr_3). While six of the nine chloroform breath samples above the detection limit were part of the high water concentration group, the values were between 1 and 3 $\mu\text{g/m}^3$, except for a single breath concentration of 12 $\mu\text{g/m}^3$, which

Table 1. Descriptive statistics of concentrations in water

	Concentration in water ($\mu\text{g/l}$)						
	CHCl_3	BDCM	CDBM	CHBr_3	TTHM	DCAA	TCAA
Mean	31	5.7	2.0	0.73	33.	19	18
Median	16	2.6	1.4	0.45	8.0	6.0	5.7
SD	46	8.6	2.1	0.90	52	24	26
Minimum	0.04	0.06	0.14	0.03	0.03	0.33	0.25
Maximum	200	48	9.7	4.21	260	110	120

Abbreviations: SD, standard deviation; BDCM, bromodichloromethane; CDBM, chlorodibromomethane; TTHM, total trihalomethane; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid.

Table 2. Comparison of air trihalomethane (THM) concentrations between the low and high water concentration groups

		THM air concentrations ($\mu\text{g}/\text{m}^3$)			
		CHCl_3	BDCM	CDBM	CHBr_3
Low water concentration group	Mean \pm SD	$0.44 \pm 0.55^*$	0.38 ± 0.82	0.44 ± 0.95	0.29 ± 0.93
	Median	0.20	0.05	0.17	0.06
	<i>n</i>	25	25	25	25
	>DL ^a	16	12	5	8
High water concentration group	Mean \pm SD	4.46 ± 6.54	0.75 ± 0.96	0.53 ± 0.84	0.35 ± 0.94
	Median	1.25	0.32	0.16	0.04
	<i>n</i>	23	23	23	23
	>DL ^a	23	16	7	4

Abbreviations: BDCM, bromodichloromethane; CDBM, chlorodibromomethane; SD, standard deviation.

^aNumber exceeding the detection limit.^{*}Significantly different between the two groups ($p = 0.0002$) using the Mann-Whitney test.**Table 3.** Mean (median) trihalomethane breath concentrations ($\mu\text{g}/\text{m}^3$) following a shower by group divided into low and high water concentrations groups

Group	Time breath sample collected after end of shower (min)	Water concentration ($\mu\text{g}/\text{l}$)	No.	CHCl_3	BDCM	CDBM	CHBr_3
A ^a	<5	Low	6	4.0 (1.3)*	1.4 (nd)*	1 (nd)*	0.6 (nd)*
		High	7	54 (59)	10 (11)	4.8 (3.6)	2.3 (2.8)
B ^b	5–20	Low	7	1.5 (1.5)*	0.3 (nd)*	1 (nd)	0.6 (nd)
		High	7	134 (20)	13 (5.9)	2.8 (0.84)	1.2 (nd)
C ^c	>20	Low	4	1 (nd)	0.3 (nd)	1 (nd)	0.6 (nd)
		High	2	20 (–)	0.3 (nd)	1 (nd)	0.6 (nd)

Abbreviations: BDCM, bromodichloromethane; CDBM, chlorodibromomethane; nd, not determined because more than half the values were below the detection limit.

^aGroup A, breath sample collected within 5 min of showering.^bGroup B, breath sample collected within 5–20 min of showering.^cGroup C, breath sample collected 20 min or more after showering.^{*}Statistically different between the two groups ($p < 0.05$) using the Mann-Whitney test.

was associated with the home with the single highest water concentration of 200 $\mu\text{g}/\text{l}$. Due to the small numbers of detectable levels, no statistically significant difference in breath concentrations could be determined between the high and low water concentration groups.

One potential reason for the lack of a clear relationship between background breath concentrations and water concentration is the rapidity at which chloroform and the other THMs are metabolized in the body. This rapid metabolism results in a rapid decline in THM body burden and, therefore, breath concentration following any exposure. Ingested THMs at environmental concentrations are completely metabolized during the first pass through the liver, whereas inhalation and dermal exposures received during showering and bathing return to background levels within a few hours (27,31).

To assess whether inhalation exposure from the indoor air was potentially occurring in the homes, air samples were collected during the time of the home visit. The sample duration was only 15 min, so it does not represent a continuous exposure estimate as was collected during the TEAM study, but it can provide some information

on the background air concentrations within the homes. Twenty-five valid air samples were collected in the low water concentration group and 23 in the high water concentration group. The mean air concentrations for each of the THMs were higher in the high water concentration group than the low, but only statistically so for CHCl_3 (Table 2). The lack of a statistically significant difference for the brominated THMs between the two groups is probably due to the generally low water concentrations for all of these compounds across the entire population. The overall median (range) of chloroform air concentrations, 0.4 $\mu\text{g}/\text{m}^3$ (<0.1–25 $\mu\text{g}/\text{m}^3$), is lower than that observed in the TEAM study, which reported a median (range) of 3 $\mu\text{g}/\text{m}^3$ (0.09–53 $\mu\text{g}/\text{m}^3$) (37), again consistent with the lower water concentrations measured in the current study. The chloroform air concentrations in both studies were correlated with the water concentration, with the current work having a Pearson product moment correlation coefficient (r) of 0.503 ($p = 0.0003$) and a Spearman rank correlation coefficient (r_s) of 0.557 ($p < 0.0009$). The relationship between the short-term chloroform air concentration (15 min) and water concentration is consistent with the

Table 4. Correlation coefficients (r^2) between the water trihalomethane (THM) concentration or THM exposure with the exhaled breath concentration (Pearson coefficient/Spearman coefficient)

	Breath vs. water	Breath vs. exposure
Group A ^a		
CHCl_3	0.782*/0.685*	0.824*/0.768*
BDCM	0.742*/0.841*	0.667*/0.786*
CDBM	0.663*/0.743*	0.398/0.651*
CHBr_3	0.974*/0.894*	0.929*/0.895*
Group B ^b		
CHCl_3	0.688*/0.785*	0.730*/0.799*
BDCM	0.273/0.789*	0.161/0.757*
CDBM	0.021/0.376	0.115/0.236
CHBr_3	0.116/-0.176	0.193/-0.262

Abbreviations: BDCM, bromodichloromethane; CDBM, chlorodibromomethane.

^aGroup A, breath sample collected within 5 min of showering.^bGroup B, breath sample collected within 5–20 min of showering.^{*}Significantly correlated each other with $p < 0.05$.

water being the source of these compounds to the indoor air.

To further evaluate the water and breath concentration relationships, each subject was asked to collect a breath sample after showering. Valid samples were obtained from 33 subjects. However, the subjects' interpretations of exactly when to collect the sample varied from immediately after the shower to 20 min later. The time delay between the exposure (shower) and when the breath sample was collected is an important determinant of the breath concentration because THM breath concentrations decline exponentially after an exposure ceases (31). Each subject was therefore assigned into one of three groups depending upon when they indicated that they collected the breath samples in a follow-up questionnaire: 1) immediately (within 5 min after showering); 2) 5–20 min (after drying off and before leaving the bathroom); and 3) >20 min (after leaving the bathroom). Thirteen samples were assigned to Group A, 14 to Group B, and 6 to Group C. However, each of these groups still contained a broad range of lag times during which the breath concentration would change significantly, thus weakening the expected association.

For the three groups, the breath concentrations collected after the showers were compared to both the water concentration and an estimate of the exposure, calculated as the product of the duration of a shower from the questionnaire and the water concentration of each THM (Table 3).

Chloroform and BDCM, the two most abundant THMs in the water, were significantly correlated for breath and water concentrations and for breath concentration and exposure for Groups A and B (Table 4). Significant correlations for CDBM and

Table 5. Comparison of urinary excretion between low and high exposure groups

		Water concentration (μg/l)	FMU excretion rate (ng/mg)	FMU Cn-norm concentration (ng/min)	VU Cn-norm concentration (ng/mg)
DCAA					
Low exposure ^a	Mean ± SD	1.76 ± 1.94	1.04 ± 0.99	1.45 ± 1.54	1.40 ± 1.34
	Median	0.69	0.73	0.72	0.87
	n	23	23	23	22
	p-Value ^b	—	0.1	0.2	—
High exposure ^a	Mean ± SD	32.7 ± 26.4	1.47 ± 1.51	1.79 ± 1.59	1.82 ± 1.56
	Median	31.1	1.08	1.23	1.38
	n	19	19	19	22
TCAA					
Low exposure ^a	Mean ± SD	1.94 ± 1.99	4.73 ± 4.02*	6.35 ± 6.45*	9.78 ± 14.9
	Median	0.82	3.26	4.30	6.00
	n	23	23	23	22
	p-Value ^b	—	0.01	0.02	—
High exposure ^a	Mean ± SD	27.6 ± 29.0	10.2 ± 7.99	10.3 ± 7.00	8.22 ± 5.56
	Median	18.7	8.44	9.40	6.81
	n	19	19	19	22

Abbreviations: DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; FMU, first morning urine; VU, time of visit urine; Cn-norm, normalized to creatinine; SD, standard deviation.

^aThe water DCAA and TCAA concentrations were significantly different due to selection criteria.

^bp-Value for comparison of low to high water concentration groups.

*Statistically different between the low and high water concentration groups at $p < 0.05$ using the Mann-Whitney test.

bromoform were found for the Group A participants but not for Group B, which is probably a function of the concentrations being near the detection limit for Group B, thus, the analytical variability in the values could mask any trend in the data. Although high correlations were calculated for Group C, only six participants were included in that group; thus, the statistical significance is questionable and these values are not included in the presentation of correlation coefficients (Table 4). The breath concentrations of participants of Group C showed no elevation when the THM concentrations in water were nondetectable; slightly elevated breath concentrations for subjects with measurable water concentrations; and a high breath concentration for the subject with a high water chloroform concentration. The observed correlations between the individual THM water and breath concentrations after a shower are consistent with showering being a source of THM exposures. The correlation coefficients calculated for breath concentrations and water concentrations and for breath concentrations and exposure were nearly identical. This suggests that the water concentration is a more important determinant of breath concentration than variations in the reported duration of showers. This is consistent with the water concentrations varying over two orders of magnitude while the shower duration varied within a factor of three. Further, shower duration was based on a recall questionnaire that introduces uncertainty in the duration reported. A stepwise regression analysis was done using exhaled breath concentrations of each THM as the dependent variable and the water concentrations, subjects' average

shower durations, water temperature (hot, warm, cold), presence of an exhaust fan, and window opened or closed as the independent variables. Shower duration and water temperature have been shown to be important factors contributing to the breath concentrations during controlled experiments (31). Only the water concentration was selected as a predictive variable of chloroform breath concentration. It is likely that the variations in the time when the breath sample was collected relative to the end of the exposure within each group introduced sufficient variability in the measured breath concentrations to preclude the contribution of shower duration and water temperature to the breath concentration from being selected in the regression analysis. Future field studies need to document the time period between the collection of biological samples and a THM exposure to obtain maximum information from those biomarkers.

DCAA and TCAA exposure and biomarkers. First morning urine samples were obtained from 47 of the 49 participants. However, five of the samples were not included in the data analysis because either the times reported indicated that the samples were not actual first morning urine samples or the urine volumes were smaller than would be expected for a complete first morning urine void. This resulted in 23 urine samples being obtained from the low water concentration group and 19 urine samples from the high water concentration group.

While neither the DCAA first morning urinary excretion rates nor the DCAA creatinine-normalized concentrations were significantly different between the two groups, the TCAA urinary excretion rates and creatinine-

normalized concentrations were (Table 5). To establish the validity of urinary TCAA as a biomarker of exposure, we examined the correlation coefficient between the water concentration, as a surrogate for exposure, and the urinary excretion rate and the creatinine-normalized concentration. No significant correlation between the water concentrations and either the urinary excretion rate or creatinine-normalized concentration of DCAA and TCAA were identified, indicating no dose-response relationship. Two possible explanations for the lack of a statistically meaningful correlation coefficient are that either TCAA and DCAA urinary excretions are not valid biomarkers of DBP exposure from drinking water or the water concentration is not a good measure of exposure.

To evaluate which explanation is correct, we calculated exposure estimates of DCAA and TCAA for the participants. We assumed that ingestion exposure was the primary exposure route because HAAs are nonvolatile and have minimum inhalation exposure. HAAs also have low skin permeability and minimal dermal absorption (33). We calculated the ingestion exposure from the measured residential DCAA and TCAA drinking water concentrations and the quantity of beverages prepared from water ingested by the participants during the previous 48 hr, as reported in a recall questionnaire administered at the time of the home visits. Some of the beverages consumed were prepared after boiling the water. Kim (38) determined that boiling water did not change the DCAA concentration significantly, after adjusting for the change in water volume due to evaporation, but the TCAA concentrations decreased by an average of 39%. Therefore, the water TCAA concentrations in hot liquids were adjusted by multiplying the original drinking water concentration by 0.61. Some of the homes also had filters on their kitchen taps. An average removal efficiency of 70% for DCAA and TCAA was calculated using paired water samples from six homes (38).

The DCAA and TCAA ingestion exposures for each subject were then calculated using the following equations:

$$EXP_{DCAA} = \text{WaterConc} \times 0.3 \text{ (if filtered)} \times (\text{VolCold} + \text{VolHot}) \quad (1)$$

$$EXP_{TCAA} = \text{WaterConc} \times 0.3 \text{ (if filtered)} \times (\text{VolCold} + 0.61 \times \text{VolHot}) \quad (2)$$

where EXP = ingestion exposure, $WaterConc$ = cold water concentration measured at home, $VolCold$ = total volume of cold liquids ingested, and $VolHot$ = total volume of hot liquids ingested.

We evaluated the strengths of the relationships between the ingestion exposure and urinary excretion using linear regression analysis, with urinary excretion rate as the dependent variable and the exposure as the independent variable. The TCAA urinary excretion rate was statistically related to the ingestion exposure with an adjusted r^2 of 0.532 ($p < 0.0001$) (Fig. 1). Because the selection criteria resulted in the data not being normally distributed, which could result in a few high values causing an anomalously high r^2 value, the regression analysis was repeated without the eight (20%) highest water concentration homes. The relationship was still statistically significant, although with a lower adjusted r^2 of 0.312 ($p < 0.0001$). The DCAA urinary excretion rate was not linearly related to the exposure, with an adjusted r^2 of -0.00545 ($p = 0.4$) (Fig. 2).

A factor that could lead to incorrect exposures being calculated for some subjects was that some subjects consumed beverages prepared with water obtained outside their homes, which had an unknown TCAA concentration. To determine whether this reduced the strength of the relationship observed between exposure and the biomarker, the regression analysis was also performed for the subset of 25 subjects who did not work outside homes during the 48 hr prior to sample collection. The linear regression between TCAA urinary excretion rate and ingestion exposure for this subgroup was stronger than for the entire cohort (adjusted $r^2 = 0.655$; $p < 0.0001$; Fig. 3) and excluding the homes with the five (20%) highest water concentrations did not reduce the strength of the association (adjusted $r^2 = 0.721$; $p < 0.0001$). The relationship between urinary excretion rate and exposure for DCAA was also examined for

this subgroup of the study population, and again no statistically significant relationship was identified (adjusted $r^2 = -0.01$; $p = 0.4$; Fig. 4). Thus, the urinary TCAA excretion rate demonstrates a dose-response relationship with exposure and therefore appears to be a valid biomarker of TCAA ingestion exposure from chlorinated water during routine household use over a 48-hr time period, whereas urinary DCAA does not. The probable reason urinary DCAA is not correlated with its exposure is its short biological residence time (< 2 hr) compared to the time interval between urinations and the use of a 48-hr time frame to calculate the ingestion exposure (39).

The lack of an association between DCAA exposure and its proposed biomarker has an underlying premise similar to that of the weak association observed between the background THM breath levels and exposure. The biological residence times of THMs are also short (minutes to hours) due to their rapid metabolism, whether ingested or via inhalation/dermal exposure during showering, and the time interval between exposures from those routes were hours (ingestion) to a day (showering). The continuous inhalation exposure from breathing indoor air is smaller than the other exposure routes. In contrast to the background breath concentrations, a true association was identified between post-shower breath concentrations and exposure, when the lag time for the breath sample collection was included. This documents that, for biomarkers of compounds with biological residence times significantly shorter than the time period between exposure and collection, it is critical to account for changes in biomarker concentrations that can occur during that time period.

We also examined the linear regression relationship between the water concentration, as a surrogate for exposure, and the urinary excretion rate (dependent variable) for both TCAA and DCAA for the subset of 25 subjects who did not work outside the home and for which a strong relationship for TCAA exposure was identified. The water concentration did not have a statistically significant relationship with the excretion rate for either compound (adjusted $r^2 = -0.04$; $p = 1$ for TCAA; Fig. 5 and adjusted $r^2 = -0.04$; $p = 0.8$ for DCAA; Fig. 6). This suggests that using the water concentration as a surrogate for ingestion exposure to DBPs from drinking water introduces exposure misclassifications.

DBP biomarkers and exposure metrics.

Exhaled breath concentrations have been found to be a biomarker of THM exposure, particularly following inhalation and dermal exposures, which usually occur for short periods. However, with the declining THM water concentrations due to lower regulatory standards and increased public health concerns, background exhaled breath concentrations have declined and will require increasingly more sensitive methods to be useful indicators of population exposures. Water concentration appeared to be a good estimate of the THM exposure associated with showering for the studied population. This is due to the greater variability in the water concentration across different water systems and time of the year than the variability in the duration and water temperature of a shower. However, this study was not a population-based study because the extreme ends of a water concentration distributions were preselected and breath samples were collected solely from females within a fairly

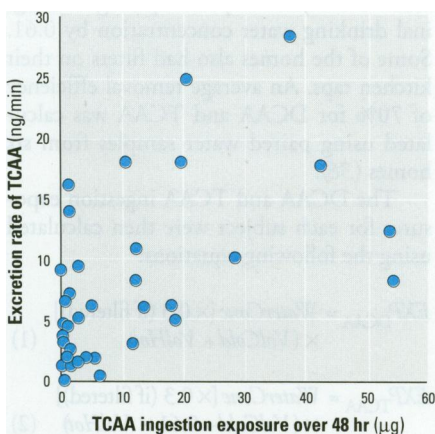


Figure 1. A scatter plot showing significant correlation between trichloroacetic acid (TCAA) ingestion exposure and the TCAA urinary excretion rate for the first morning urine samples from all subjects from which a first morning urine sample was obtained ($n = 42$).

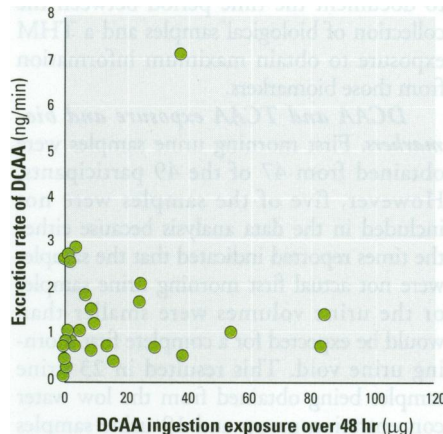


Figure 2. A scatter plot showing no significant correlation between dichloroacetic acid (DCAA) ingestion exposure and the DCAA urinary excretion rate for the first morning urine samples from all subjects from which a first morning urine sample was obtained ($n = 42$).

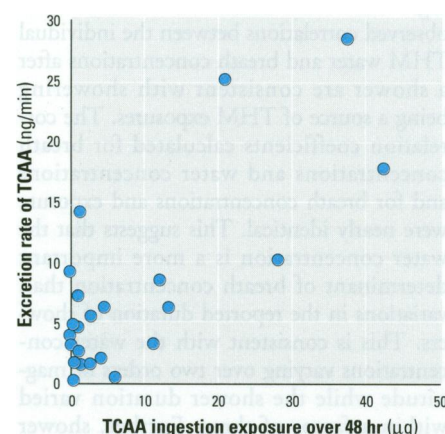


Figure 3. A scatter plot showing significant correlation between trichloroacetic acid (TCAA) ingestion exposure and the TCAA urinary excretion rate for the first morning urine samples from subjects who only ingested water at home ($n = 25$).

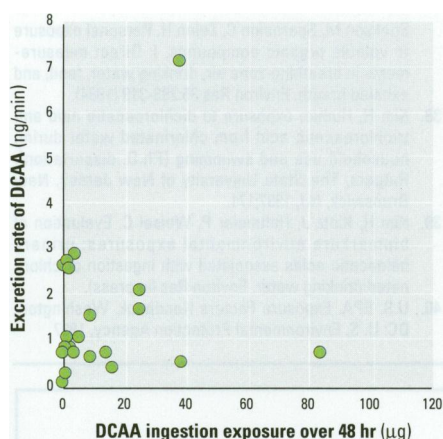


Figure 4. A scatter plot showing no significant correlation between the dichloroacetic acid (DCAA) ingestion exposure and the DCAA urinary excretion rate for the first morning urine samples from subjects who only ingested water at home ($n = 25$).

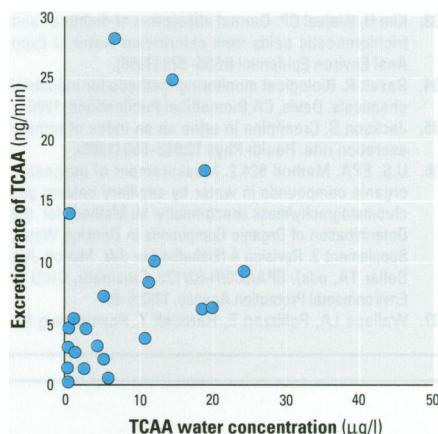


Figure 5. A scatter plot showing no significant correlation between the trichloroacetic acid (TCAA) water concentration and the TCAA urinary excretion rate for the first morning urine samples from subjects who only ingested water at home ($n = 25$).

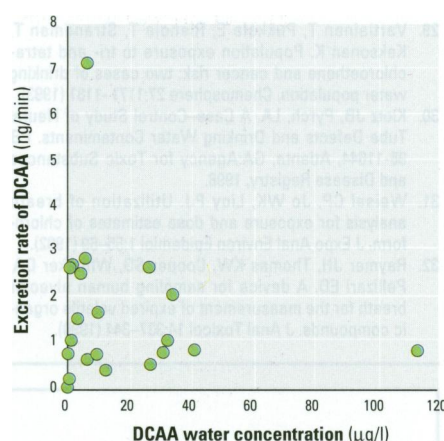


Figure 6. A scatter plot showing no significant correlation between the dichloroacetic acid (DCAA) water concentration and the DCAA urinary excretion rate for the first morning urine samples from subjects who only ingested water at home ($n = 25$).

narrow age range. The variability in the duration of showering within the population is larger than in the current study. Different age groups and genders have different showering habits, and not all individuals shower or bathe daily while others shower longer than 30 min/day, the upper duration for the study population (40). Thus, it is possible that water concentration would not be as good a surrogate for THM exposure in a population-based sample as was found for the current study population, which consisted of only female individuals of a narrow age range.

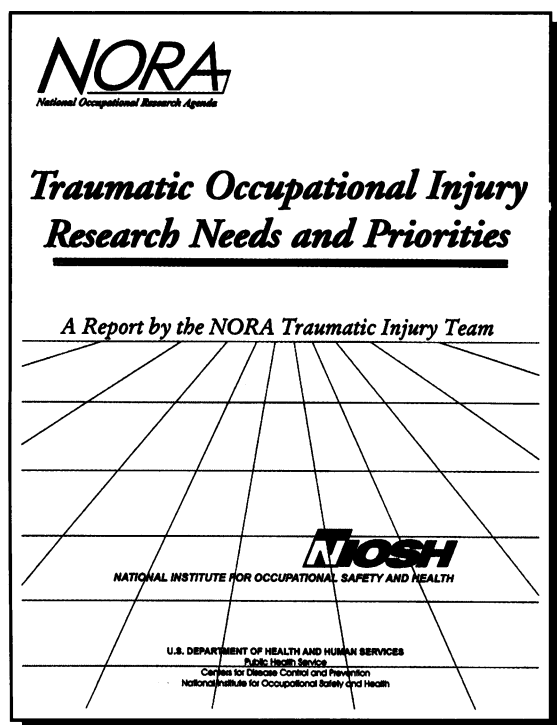
The urinary TCAA excretion rate and creatinine-normalized concentrations were identified as good biomarkers of chronic ingestion exposure, but DCAA was not. Water concentration was not a good surrogate for TCAA exposure. One explanation may be the large variability in the amount of chlorinated water and beverages prepared from water consumed across the population. Further, because individuals consume chlorinated water from various sources, the assignment of a single value to the water concentration consumed may have resulted in increased misclassification of exposure. It is important for epidemiologic studies of exposure to nonvolatile DBPs, for which ingestion is the dominant route, to consider sources and quantities of the water, beverages, and food containing water consumed when assigning an exposure value to minimize misclassification. This may be less important for DBPs that have inhalation and dermal exposures from showering as major contributions because it is less likely that showers occur away from the home, with the probable exception of athletes and swimmers who receive exposures in chlorinated swimming pools.

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NIOSH Publishes Occupational Injury Research Strategy



The report *Traumatic Occupational Injury Research Needs and Priorities* was recently published by the National Institute for Occupational Safety and Health (NIOSH). The report covers one of the 21 priority areas identified as a part of the National Occupational Research Agenda (NORA), an effort by NIOSH to develop a framework to guide occupational health and safety research for the next decade. The report was prepared by a team of experts from government, industry, labor, and academia, and covers research objectives in the areas of surveillance, analytic injury research, prevention and control, implementation, and evaluation.

Copies of the report, DHHS (NIOSH) Publication No. 98-134, may be obtained from NIOSH Publications Dissemination, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 USA, 1-800-356-3674, fax: 513-533-8573, e-mail: pubstaft@cdc.gov.